IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant(s): Martis et al.
Appl. No.: 09/955,248
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Title: BIOCHEMICALLY BALANCED PERITONEAL DIALYSIS SOLUTIONS
Art Unit: 1621
Examiner: R. Keys
Docket No.: DI-4641 CONT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' REPLY BRIEF

Sir:

I. INTRODUCTION

Appellants submit Appellants' Reply Brief in response to Examiner's Answer dated November 19, 2003 pursuant to 37 C.F.R. § 1.193(b)(1). Appellants respectfully submit the Examiner's Answer has failed to remedy the deficiencies with respect to the Final Office Action dated January 14, 2003 as noted in Appellants' Appeal Brief filed on August 6, 2003 ("Appeal Brief") for the reasons set forth below. Accordingly, Appellants respectfully request that the rejections of the pending claims be reversed.

II. CLAIMS 1-16 DO NOT STAND OR FALL TOGETHER

Appellants believe that Claims 1-16 do not stand or fall together contrary to the Patent Office's position. See, Examiner's Answer, page 2. At the outset, Appellants' Appeal Brief includes a statement that the grouping of the claims does not stand or fall together. Indeed, the Appeal Brief under the heading VII. GROUPING OF THE CLAIMS on page 6 provides as follows:

> [a]ppellants argue for the separate patentability of each of the independent claims separate and apart from each other set forth in detail below pursuant to the requirements of 37 C.F.R. §1.192 (7), unless otherwise specified.

Appeal Brief on pages 6 and 7, each of the independent claims is separately described. Claims 1, 6, 10 and 11 each recite peritoneal dialysis solutions that require different concentrations regarding the combination of carbon dioxide partial pressure, weak acid and bicarbonate. Indeed, Claim 11 recites a method for correcting metabolic acidosis.

Moreover, in response to the anticipation rejections, a separate discussion of each of independent Claims 1 and 6 is provided, for example, in the argument section of the Appeal Brief on pages 11-13, and in response to the obviousness rejections, a separate discussion of each of independent Claims 1, 6, 10 and 11 is provided, for example, in the argument section of the Appeal Brief on page 13. At a minimum, this clearly demonstrates Appellants' intent to argue for the separate patentability of each of independent Claims 1, 6, 10 and 11. Indeed, Appellants have continued to argue in this way in response to the Examiner's Answer as provided below. Therefore, Appellants believe the Patent Office's statement that pending Claims 1-16 stand or fall together is both improper and unfair.

III. *SCHAMBYE* AND *VEECH I* FAIL TO ANTICIPATE THE CLAIMED PERITONEAL DIALYSIS SOLUTIONS OF CLAIMS 1, 2 and 4-8

Appellants respectfully submit that the peritoneal dialysis solutions as defined by Claims 1, 2 and 4-8 are not anticipated by what *Schambye* or *Veech I* (U.S. Patent No. 4,663,166) allegedly disclose. Of pending claims 1, 2 and 4-8, Claims 1 and 6 are the sole independent claims which each relate to peritoneal dialysis solutions. The peritoneal dialysis solution of Claim 1 includes, in part, a bicarbonate concentration of less than or equal to 30 mM/L, a carbon dioxide partial pressure that is less than 60 mmHg and at least one weak acid not including acetate at a concentration between approximately 15 mEq/L and approximately 20 mEq/L. Claim 6 recites a peritoneal dialysis solution that includes, in part, a bicarbonate concentration that ranges from 20.0 mEq/L to 30.0 mEq/L, a carbon dioxide partial pressure that is less than 60 mmHg and a weak acid not including acetate at a concentration from 10 mEq/L to 20 mEq/L.

A. The claimed carbon dioxide partial pressure is not inherent

In contrast, Appellants believe that *Schambye* and *Veech I* are deficient with respect to the claimed peritoneal dialysis solutions as defined by Claims 1 and 6. At the outset, both *Schambye* and *Veech I* at least fail to disclose expressly the claimed carbon dioxide partial

pressure as even admitted by the Patent Office. See, Examiner's Answer, pages 3 and 4. Further, Appellants believe that *Schambye* and *Veech I* do not inherently disclose the claimed carbon dioxide partial pressure.

Of course, "inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Oelrich*, 212 U.S.P.Q. 323, 326 (CCPA 1981) (quoting *Hansgirg v. Kemmer*, 40 U.S.P.Q. 665, 667 (CCPA 1939). The Patent Office primarily relies on what *Schambye* and *Veech I* allegedly disclose with respect to the bicarbonate and weak acid concentrations in support of the inherency rejection. Contrary to the Patent Office's position, both *Schambye* and *Veech I* fail to provide the claimed bicarbonate and weak acid concentrations.

With respect to *Schambye*, this reference provides a bicarbonate concentration that is 20 mM or less. Indeed, *Schambye* states that "a bicarbonate concentration of 20 mM is less cytotoxic than solutions with higher lactate or higher bicarbonate concentrations..." See, *Schambye*, S118. This is clearly different from the claimed bicarbonate concentration that ranges from 20.0 mEq/L to 30.0 mEq/L as required by Claim 6. Further, *Schambye* provides that "the most advantageous CAPD solution [includes] ... a lactate concentration of 12.5 mM." Clearly, this contrasts the claimed weak acid concentration between approximately 15 mEq/L and approximately 20 mEq/L as required by Claim 1. Thus, the carbon dioxide partial pressure feature of Claims 1 and 6 is not inherent in view of *Schambye.*

With respect to *Veech I*, this reference discloses a preferred weak acid concentration in a peritoneal dialysis solution that ranges from 2 mmole/L to 10 mmole/L. See, *Veech I*, Table VI. Clearly, the preferred weak acid concentration as disclosed in *Veech I* is different than the weak acid concentration from between 15 mEq/L and approximately 20 mEq/L as required by Claim 1 or the weak acid concentration that ranges from 10 mEq/L to 20 mEq/L as required by Claim 6. Therefore, the carbon dioxide partial pressure feature of Claims 1 and 6 is not inherent in view of *Veech I.*

B. The Patent Office Has Improperly Relied on *Zander*

Moreover, Appellants believe that the Patent Office has improperly relied on *Zander* in support of the anticipation rejections. Appellants respectfully submit that it is both improper and unfair for the Patent Office to reject Claims 1, 2 and 4-8 as allegedly anticipated by *Schambye* or *Veech I* where as in this case the Patent Office has relied on *Zander* to do so. This clearly suggests the Patent Office's intent to reject Claims 1, 2 and 4-8 for alleged obviousness reasons. Indeed, these same claims are, in fact, also rejected as allegedly obvious in view of *Schambye* or *Veech I* in combination with *Zander*.

Accordingly, Appellants respectfully submit that *Schambye* or *Veech I* fail to anticipate the peritoneal dialysis solutions as required by Claims 1, 2 and 4-8.

IV. CLAIMS 1-16 ARE NOT OBVIOUS

Appellants believe that the obviousness rejections of Claims 1-16 in view of *Schambye*, *Veech I*, and *Veech II* (U.S. Patent No. 6,020,007) alone or in combination with *Zander* are improper. Contrary to the Patent Office's position, *Schambye*, *Veech I* and *Veech II* are deficient with respect to a peritoneal dialysis solution with a unique combination of bicarbonate, a weak acid and a carbon dioxide partial pressure as claimed. Indeed, this unique combination is essential to both maintain the acid-base balance of dialysis patients and further to improve biocompatibility as supported in the Declaration of Leo Martis, Ph.D. at ¶¶7-10 (refer to Exhibit F of Appellants' Appeal Brief).

A. The method for correcting metabolic acidosis of Claims 11-16 is not obvious

At the outset, Appellants believe that the Patent Office has improperly rejected Claims 11-16 for alleged obviousness in view of *Veech I* or *Veech II* in combination with *Zander*. Of pending Claims 11-16, Claim 11 is the sole independent claim. Claim 11 recites a method for correcting metabolic acidosis that includes, in part, the step of administering to a patient a peritoneal dialysis solution with a bicarbonate level and a carbon dioxide partial pressure that is substantially similar to that found in the patient's blood and further a bicarbonate concentration and a weak acid concentration that ranges from 20 mEq/L to 30 mEq/L and from 10 mEq/L to 20 mEq/L, respectively. Again, the method of Claim 11 provides a biochemically balanced

peritoneal dialysis solution that can be effectively administered to correct metabolic acidosis associated with chronic renal failure in a more physiological manner.

1. *Veech I* and *Veech II* fail to disclose or suggest the method of Claims 11-16

In contrast, *Veech I* and *Veech II* are deficient with respect to the method for correcting metabolic acidosis as required by Claim 11 for at least a number of reasons. As admitted by the Patent Office, *Veech I* and *Veech II* fail to provide a carbon dioxide partial pressure that is approximately the same as the carbon dioxide partial pressure of blood as required by Claim 11. See, Examiner's Answer, pages 6 and 8.

Further, while the *Veech* references generally disclose peritoneal dialysis solutions, both references fail to disclose or suggest peritoneal dialysis solutions that are capable of maintaining an acid-base balance in a long term dialysis patient. In fact, the *Veech* references do not even address the problem of metabolic acidosis in patients suffering from end stage renal failure. Indeed, the *Veech* references provide peritoneal dialysis solutions with bicarbonate and weak acid concentrations that are too broad and cover too many inoperative solutions that would result in metabolic acidosis or metabolic alkalosis if used for long term peritoneal dialysis solutions.

In this regard, *Veech I* discloses peritoneal dialysis solutions with bicarbonate and weak acid concentrations that broadly range from 0 mmole/L to 60 mmole/L. *Veech I* even discloses preferred peritoneal dialysis solutions that broadly range in bicarbonate concentration from 25 mmole/L to 45 mmole/L and weak acid concentration from 2 mmole/L to 10 mmole/L. See, *Veech I*, Table VI. With respect to *Veech II*, the Patent Office principally relies on its teachings regarding a Type C solution that is allegedly suitable for use in peritoneal dialysis. See, Examiner's Answer, page 8. The bicarbonate and weak acid concentrations of the Type C solution can broadly range from 0-40 mMole/L and 0-55 mMole/L, respectively, as disclosed in *Veech II* at Table II.

Indeed, at bicarbonate concentrations that are considerably in excess of normal as disclosed in the *Veech* references, a partial pressure of carbon dioxide that is at least twice the physiologic partial pressure of carbon dioxide (e.g., greater than 80 mmHg) is required in order to maintain the peritoneal solution at a physiological pH. Although such a solution may meet the metabolic needs of the patient, such as solution does not provide a physiological environment for the peritoneal cells in contact with the solution. Due to the differences in transport rates between

bicarbonate and carbon dioxide, with such a solution, the intracellular hydrogen ion concentration of the cells lining the peritoneal cavity, as well as those present in the peritoneal cavity, would be severely low placing them at a metabolic disadvantage. This metabolic disadvantage will increase more than would be expected if they share the extracellular environment of normal pH, but a supernormal bicarbonate and partial pressure of carbon dioxide. See, Appellants' Appeal Brief , V. Summary of Invention, at pages 3 and 4 (referring to Appellants' Specification, page 3, lines 16-23.) Thus, the *Veech* references fail to address the problem of metabolic acidosis.

This clearly contrasts the method for correcting metabolic acidosis as required by Claim 11. The method of Claim 11 requires administering a peritoneal dialysis solution at least having weak acid and bicarbonate concentrations that range from 10 mEq/L to 20 mEq/L and from 20 mEq/L to 30 mEq/L, respectively. Indeed, the bicarbonate and weak acid concentrations of Claim 11 are clearly different than the bicarbonate and weak acid concentrations as broadly defined in the *Veech* references and discussed above. As previously discussed, the unique combination of bicarbonate, a weak acid not including acetate and carbon dioxide partial pressure at specified concentrations provides a peritoneal dialysis solution that can be effectively administered to maintain the acid-base balance in a peritoneal dialysis patient suffering from end stage renal disease as required by Claim 11. Moreover, the efficacy and safety of the claimed peritoneal dialysis solutions have been proven in a clinical study as supported in the Declaration of Leo Martis, Ph.D. at ¶¶7-10. Therefore, Appellants believe that *Veech I* and *Veech II*, even if combinable, are clearly deficient with respect to the claimed method for correcting metabolic acidosis as required by Claims 11-16.

2. *Zander* cannot remedy the deficiencies of *Veech I* and *Veech II*

Moreover, Appellants do not believe that the Patent Office can rely solely on *Zander* to remedy the deficiencies of *Veech I* and *Veech II*. The Patent Office merely relies on *Zander* for its alleged teachings regarding carbon dioxide partial pressure in peritoneal dialysis solutions. Yet, the *Zander* patent is not credible and the solutions in the *Zander* patent suggest that no thought has been given to the buffer content required to maintain the acid-base balance as supported by the Declaration of Leo Martis, Ph.D. at ¶¶ 4-6. Therefore, Appellants do not believe that one skilled in the art would be inclined to modify *Veech I* or *Veech II* to provide a

peritoneal dialysis solution with the unique combination of carbon dioxide partial pressure in addition to bicarbonate and weak acid that can be effectively administered to correct for metabolic acidosis as required by Claims 11-16.

Accordingly, Appellants believe that Claims 11-16 are not obvious in view of *Veech I*, *Veech II* and *Zander*, even if combinable.

B. The Peritoneal Dialysis Solutions of Claims 1-10 are not obvious

Appellants believe that the obviousness rejections of Claims 1-10 in view of *Schambye*, *Veech I* and *Veech II* alone or in combination with *Zander* are improper. Contrary to the Patent Office's position, *Schambye*, *Veech I* and *Veech II* are deficient with respect to the unique combination of bicarbonate, a weak acid and a carbon dioxide partial pressure as claimed. Of pending claims 1-10, Claims 1, 6 and 10 are the sole independent claims. Claims 1 and 6 recite peritoneal dialysis solutions as previously discussed. Claim 10 recites a peritoneal dialysis solution that includes, in part, a weak acid (not including acetate) at a concentration from 10 mEq/L to 20 mEq/L, a bicarbonate concentration from 20 mEq/L to 30 mEq/L, a carbon dioxide partial pressure that is similar to the partial pressure of a normal subject's blood, and a pH of approximately 7.0 to about 7.4.

With respect to *Schambye*, this reference is deficient with respect to the claimed carbon dioxide partial pressure features as required by Claims 1, 6 and 10 and admitted by the Patent Office. See, Examiner's Answer, pages 3 and 5. Further, *Schambye* is deficient with respect to additional features as claimed in Claims 1 and 6 as discussed above. Moreover, *Schambye* merely provides a bicarbonate concentration that is 20 mM or less. This is clearly different from the bicarbonate concentration of Claim 10 that ranges from 20 mEq/L to 30 mEq/L.

With respect to *Veech I* and *Veech II*, these references fail to provide the claimed carbon dioxide partial pressure features as further admitted by the Patent Office. See, Examiner's Answer, pages 4, 6 and 8. Further, *Veech I* and *Veech II* provide peritoneal dialysis solutions that contain a broad range of weak acid and bicarbonate concentrations that are clearly different than the weak acid and bicarbonate concentrations as required by Claims 1, 6 and 10. Again, the unique and specific combination of bicarbonate, weak acid and carbon dioxide partial pressure in a peritoneal dialysis solution as claimed is essential to maintain the acid-base balance of dialysis patients as previously discussed. Therefore, *Schambye*, *Veech I* and *Veech II*, even if combinable,

fail to disclose or suggest the peritoneal dialysis solutions with the specific and unique combination of carbon dioxide partial pressure, bicarbonate and weak acid as required by Claims 1, 6 and 10.

Further, Appellants do not believe that the Patent Office can rely solely on *Zander* to remedy the deficiencies of *Schambye*, *Veech I* and *Veech II*. Again, the Patent Office merely relies on *Zander* for its alleged teachings regarding carbon dioxide partial pressure in peritoneal dialysis solutions. Therefore, Appellants do not believe that one skilled in the art would be inclined to modify *Schambye*, *Veech I* and/or *Veech II* to provide a peritoneal dialysis solution with a carbon dioxide partial pressure concentration in addition to weak acid and bicarbonate concentrations as claimed contrary to the Patent Office's position.

Accordingly, Appellants respectfully submit that the anticipation and/or obviousness rejections of Claims 1-16 are at odds with the law and facts.

V. CONCLUSION

For the foregoing reasons, Appellants respectfully submit that the Examiner's Answer does not remedy the deficiencies noted in Appellants'Appeal Brief with respect to the Final Office Action. Therefore, Appellants respectfully once again request that the Board of Appeals reverse the rejections.

Respectfully submitted,

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